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SYNTHESIS OF QUINOLINE DERIVATIVES USING MICROWAVE IRRADIATION: THEIR ANTI-CANCER ACTIVITY

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ABSTRACT

Simple and catalyst free preparation of quinolin-6-ones were synthesized by the reaction of 4-chloro-4H-chromene-3-carbaldehyde and different amines using microwave irradiation. All the reactions were preceded smoothly by yielding good to better yields. The synthesized compounds were active against several cancer cells.

KEYWORDS: Quinoline, Amines, Microwave, Anti-Cancer Activity

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Original Article

INTRODUCTION

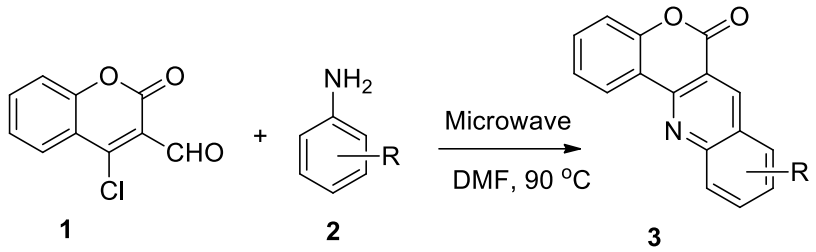
Coumarins are having diverse pharmacological activities in medicinal chemistry. Their core contains many active biological molecules used in the treatment of AIDS and cancer [13] Blend of chromene with a quinoline moiety showing great bioactivity against malignancy cell lines.

By knowing the anticancer activity of coumarins and chromenes[4], we want to synthesize quinolin-6-one derivatives by using microwave irradiation which are having anticancer properties.

For the past few years, our team was working on the development of novel methods which are reusable and on the development of pharmaceutical products including impurities. [5-10]In this paper we describe the synthesis of quinolin-6-ones utilizing microwave light alongside their cancer activity corresponding to the synthesized molecules.

RESULTS AND DISCUSSION

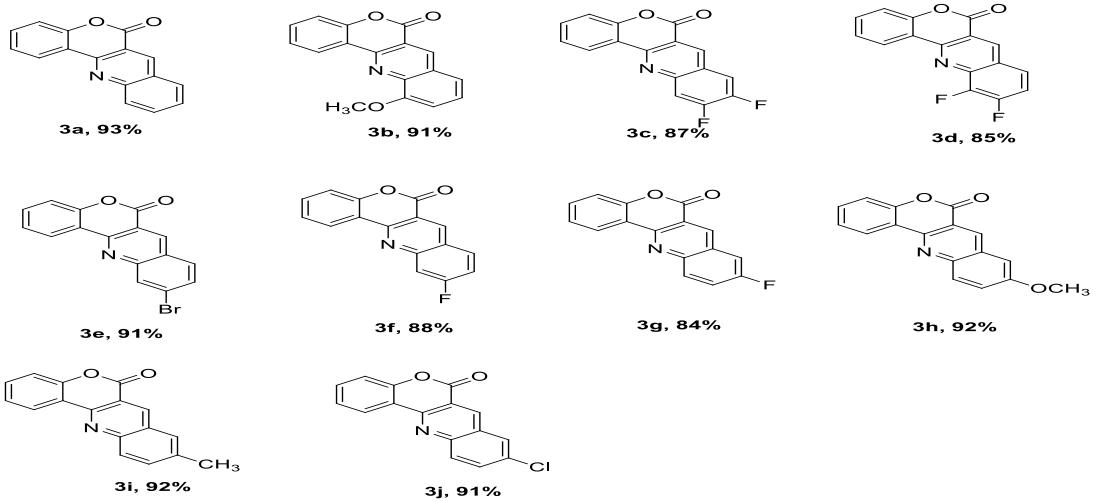
Previously, quinolin-6-ones were prepared from 4-chloro-4H-chromene-3-carbaldehyde using $AlCl_3$ as a catalyst,[11] Ultrasound[12]or *via* other methods. To overcome the disadvantages, we were keen on fostering another impetus free strategy for the amalgamation of quinolin-6-ones. For this, we developed an microwave assisted synthesis of quinolin-6-ones (**3**) by the reaction of 4-chloro-4*H*-1-benzopyran-3-carboxaldehyde (**1**) and different anilines (**2**). Primarily, we screened the reactions between aldehyde **1** with aniline (**2a**) using different solvents and found that DMF is the for this process.



Scheme 1: Preparation of quinolin-6-ones using 4-chloro-4H-chromene-3-carbaldehyde

After optimizing the reaction condition, then we screened the simplification and extent of this methodology. Thus, different amines having aromatic nature were used with aldehyde in DMF at 90 °C under microwave irradiation yielded corresponding products in good yields (Table 2). Formations of all the products are good and all the substitutions were well tolerated. There are no side product formations in the reaction. All the prepared compounds were confirmed by analytical methods.

Table 1: Synthesis of quinolin-6-ones (3) from 1under Microwave



[a]All the reactions were done by reacting **1** (1.0 mmol) and **2** (1.0mmol) under microwave

[b]Isolated yield.

Biology

All the synthesized compounds were screened against cancer activity using MTTassay and IC_{50} values of the compounds are reported in Table 1. In all the compounds 3c, **3d**, 3e, **3i**, and **3j** (IC_{50} ~<40 μM, Table 1) are found most active.

Table 2: Anticancer Activity of Compounds 3

Compound	$IC_{50}(\mu M)^a$			
	K562	Colo-205	MDA-MB 231	IMR32
3a	44	28	22	38
3b	36	34	36	48
3c	33	13	28	35
3d	26	32	32	39
3e	21	28	22	33
3f	39	31	49	48
3g	47	22	21	49
3h	36	48	29	46
3i	20	27	15	35
3j	30	15	23	32
Harmine	44	45	53	67

[a]IC_{50} represent the concentration of compound that causes a 50% growth

Inhibition to untreated cells using the MTT assay.

CONCLUSIONS

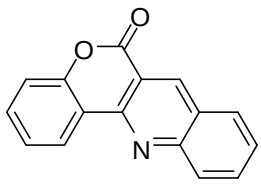
In conclusion, quinolin-6-ones was synthesized by the reaction of 4-chloro-4H-chromene-3-carbaldehyde with various aromatic amines *via* Microwave irradiation. All synthesized compounds were characterized and screened against various cancer cell lines and found active.

Experimental Section

General procedure for the preparation of quinolin-6-ones **(3):** A solution of4-chloro-4*H*-1-benzopyran-3-carboxaldehyde (1 mmol.) aromatic amine (1 mmol.) in DMF (10 ml) were kept in a 10 mL reaction vial. The reaction vial was kept under Microwave irradiation. After completion, the reaction was evaporated. The crude compound was purified from EtOH to afford the required product.

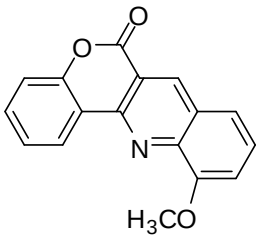
Spectral data of few Synthesized Compounds

1. Compound (3a)



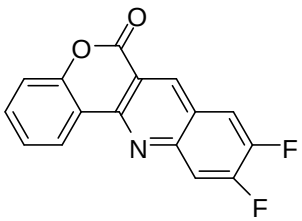
colorlesssolid; ^{1}H NMR (500 MHz, Dimethylsulphoxide-d_6):δ ppm9.35 (1H, s), 8.68 (1H, dd), 8.33 (1H, d), 8.22 (1H, d), 8.04-8.06 (1H, m), 7.67-7.78 (2H,m), 7.48-7.52 (2H, m); ^{13}C NMR (125 MHz, Dimethylsulphoxide-d_6):δ 161.2, 153.6, 151.3, 148.9, 140.9, 133.9, 132.8, 131.0, 129.6, 127.9, 127.5, 125.5, 124.9, 120.1, 118.1, 115.9; IR (cm-1): 3068, 2932, 1748, 1600, 1472, 1189; Mass: m/z 248.2 (M+).

2. Compound(3b)



colorlesssolid; ^{1}H NMR (500 MHz, Dimethylsulphoxide -d_6):δ ppm9.18 (1H,s), 8.84 (1H,dd), 7.58-7.64 (3H,m,), 7.38-7.45 (2H,m,), 7.28 (1H,d), 4.18 (3H, s); ^{13}CNMR (125 MHz, Dimethylsulphoxide -d_6):δ ppmδ 161.1, 152.8, 152.2, 150.1, 135.9, 128.9, 128.4, 126.6, 127.8, 126.8, 125.3, 123.0, 119.1, 115.1, 113.1, 57.3; IR (cm^{-1}): 3058, 2842, 1741, 1610, 1375, 1188, 764; Mass: *m*/*z*278.3 (M+).

3. Compound(3c)



colorlesssolid; ^{1}H NMR (500 MHz, Dimethylsulphoxide -d_6):δ ppm9.26 (1H, s), 8.78 (1H, dd), 7.84-7.88 (1H, m), 7.64-7.68 (1H,m), 7.41-7.58 (3H,m); ^{13}CNMR (500 MHz, Dimethylsulphoxide -d_6):δ ppm161.1, 153.2, 151.2, 141.4, 140.8, 133.4, 126.2, 125.4, 119.6, 118.4, 116.4, 116.4, 115.2, 115.1, 114.7, 114.4; IR (cm^{-1}): 3068, 2935, 1738, 1609, 1469, 1178; Mass: *m*/*z*284.2 (M+).

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